Medical Signs and Symptoms Associated with Disability, Pain, and Psychosocial Adjustment in Systemic Sclerosis

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ABSTRACT. ***Objective.*** To examine physician-assessed medical signs and patient-reported medical symptoms as correlates of 3 quality of life (QOL) outcomes in patients with systemic sclerosis (SSc): disability, pain, and psychosocial adjustment.

Methods. One hundred fourteen patients with SSc underwent a comprehensive clinical examination including determination of skin thickening [Modified Rodnan Skin Score (MRSS)]. Patients reported current symptoms and completed standardized questionnaires assessing disability and pain (Health Assessment Questionnaire) and psychosocial adjustment (Psychosocial Adjustment to Illness Scale). Regression analysis was used to examine physician-determined and patient-reported correlates of the 3 outcomes.

Results. MRSS was a significant correlate of all outcomes, although it explained only a small amount of the variance in psychosocial adjustment. Patient-reported postprandial bloating was the strongest correlate of psychosocial adjustment, explaining more than twice as much variance as MRSS. After accounting for MRSS, patient-reported dependent edema significantly correlated with all outcomes. For disability, significant correlates were physician-determined joint tenderness and number of tender points, and patient-reported joint pain on motion, joint contracture, extremity ulcers other than digital, and dyspnea. Patient-reported joint tenderness was significantly associated with pain. Regression analysis supported a model in which disability and pain mediated the relationship between MRSS and psychosocial adjustment.

Conclusion. Skin score is strongly associated with disability and pain, but only weakly associated with psychosocial adjustment. Dependent edema has negative implications across quality-of-life outcomes. Disability and pain mediate the relationship between disease severity and psychosocial adjustment to disease. Assessment (including self-report of patient symptoms) of specific medical signs and symptoms may indicate SSc patients experiencing diminished QOL. (J Rheumatol 2007;34:359–67)

Key Indexing Terms:
SCLERODERMA QUALITY OF LIFE PSYCHOSOCIAL ADAPTATION DISABILITY PAIN

Systemic sclerosis (SSc) is chronic, progressive, and debilitating, but until recently few studies have examined what specific features of the disease have the greatest influence on health-related quality of life (QOL), or which patients are at greatest risk for poor QOL outcomes[1,2]. QOL outcomes particularly relevant to SSc include disability, pain, and psychosocial adjustment. Disability has received the most systematic study. Most studies have used the self-report Health Assessment Questionnaire (HAQ)[3] or the scleroderma-modified HAQ (SHAQ)[4], both of which yield a Disability Index (HAQ-DI) that has been validated for SSc[4-13]. Generally, patients with diffuse cutaneous SSc (dcSSc) report greater disability than patients with limited cutaneous SSc (lcSSc), and more skin thickening (assessed by skin score) is associated with greater disability[4,5,11,14-17], although a recent French study did not find these relationships[18]. Considering more specific clinical signs, HAQ-DI has been shown to be related to joint pain, swelling, and/or tenderness[4,5,7,8], proximal muscle weakness[5], loss of hand mobility[5,11], presence of tendon friction rubs[5], and heart/kidney involvement[4]. Two recent studies have found digital ulcers are related to higher disability[10,11], although an earlier study did not find this relation-

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ship[5]. Virtually all these studies have relied on clinical examination and laboratory findings, and few have included patients' reports of their specific disease-related symptoms. In an exception, Smyth, *et al* had patients use visual analog scales (VAS) to rate "interference with function" of several aspects of disease, and found all ratings significantly correlated with HAQ-DI in expected directions[11]. These results suggest the importance of directly surveying patients about their disease-related symptoms.

Despite widespread agreement that pain is a central characteristic of SSc, and the importance of identifying specific disease characteristics associated with pain[1,2,9,17], there are few studies of pain correlates. Existing studies have mainly relied on the VAS self-rating of pain (PVAS) that is part of the HAQ. HAQ-PVAS scores have shown significant relationships to joint pain, digital ulcers, heartburn, and tendon friction rubs[4], and to digital ulcers[10]. In the most comprehensive study to date of pain in SSc, patients with diffuse and limited disease did not differ in their scores on a pain questionnaire; unfortunately, this study did not examine specific disease signs and symptoms as predictors of pain[17]. Thus, we know little about what aspects of disease are most strongly related to patients' experiences of pain.

A third important QOL outcome is psychosocial adjustment[1,2]. Most studies have focused on depression as a specific indicator of adjustment, and found evidence of elevated levels of depressive symptoms in patients with SSc[16-24]. Only a few studies have examined psychosocial adjustment as a broader QOL variable rather than as specific depressive symptoms; these studies have documented adjustment problems on the Psychosocial Adjustment to Illness Scale (PAIS)[15,25,26]. There has been little systematic examination of the relationship of disease signs and symptoms to psychosocial outcomes, and here again studies have mainly focused on depression. One study provided evidence that patients with digital ulceration may be more at risk for depression[19]. Although this study did not find gastrointestinal (GI) involvement was correlated with depression, using a simple yes/no indicator, another study did find evidence for a relationship between overall GI dysfunction (in particular, upper tract) and depression[22]. A French study found depression was higher in patients with pulmonary restrictive disease[18]. Finally, a study in Japan reported that most disease severity variables (including skin score and organ involvement) did not relate to depressive symptoms; however, many of the specific findings were not presented[23]. Little is known about the medical correlates of the broader variable of psychosocial adjustment, although disease severity (measured as skin score) was correlated with psychosocial adjustment in 2 studies[15,25]. Results are mixed as to whether patients with dcSSc versus lcSSc have more adjustment problems[15,17]. Finally, no studies of psychosocial adjustment outcomes have systematically examined patient-reported symptoms as predictors.

Identifying which specific clinical signs and patient-reported symptoms of SSc are indicative of poorer QOL outcomes is essential to screen patients who may be having difficulties managing their disease. In this study we examined medical correlates (based on physician clinical examination and patient report) of disability, pain, and psychosocial adjustment. Consistent with previous literature, we hypothesized that overall disease severity (expressed as skin score) would correlate with QOL outcomes. Given previous findings that the 3 QOL outcomes are interrelated[1,2], to further explore the structure of relationships among these outcomes we tested 2 different mediational models: (1) pain and disability mediate the relationship between disease severity and psychosocial adjustment; or alternatively, (2) pain and psychosocial adjustment mediate the relationship between disease severity and disability. The first model hypothesized that medical signs and symptoms would have strong direct relationships with disease-related pain and disability, and that these variables in turn would have strong direct relationships with psychosocial adjustment. The second model hypothesized that medical signs and symptoms would have strong direct relationships with disease-related pain and psychosocial adjustment, and that these variables in turn would have strong direct relationships with disability.

MATERIALS AND METHODS

This cross-sectional sample of patients was recruited through registries maintained at the Divisions of Rheumatology at UCSD and UCLA Schools of Medicine, and the Virginia Mason Medical Center (VMMC), as well as through clinical practices of the investigators. Individuals were recruited on the basis of a physician-confirmed diagnosis of SSc and a willingness to participate in studies focusing on the medical and psychosocial aspects of SSc. In addition, participants were required to be 10 years or less from onset of first non-Raynaud's symptoms. Exclusionary criteria included the presence or history of: rheumatoid arthritis, systemic lupus erythmatosus, dermatomyositis, linear scleroderma/morphea, eosinophilic fasciitis/eosinophilia-myalgia syndrome, vasculitis, breast implants, cancer treatments in the previous 3 years, serious neurologic disease, and/or acquired immune deficiency syndrome. Prospective participants were contacted by physicians, nurse practitioners, or study coordinators; 89% of those contacted enrolled in the study. The study had full institutional review board approval at all 3 medical institutions, plus the home institution of the first author. Participants received clinical examinations by physician investigators, and then completed questionnaires. Participants either completed the questionnaires onsite or returned completed questionnaires by mail within 2 weeks.

The extent and severity of skin thickening was quantified as Modified Rodnan Skin Score (MRSS) during the clinical evaluation[27,28]. The MRSS is a valid measure of disease severity in SSc[14,27,28]. Skin thickness in 17 body surface areas is assessed by clinical palpation using a 0–3 point scale (0 = normal, 1 = mild, 2 = moderate, 3 = severe). The MRSS is the sum of scores for all 17 body areas (maximum = 51). Total scores range from 0 to 51, with higher scores representing more severe and widespread skin thickening. A variety of physician-determined clinical data were also obtained, including those listed in Table 3. Several summary indices were determined: Proximal muscle weakness was rated on a 0 (not present) to 4 (profound) scale. Total tendon friction rubs were quantified by determining the presence (1) or absence (0) of rubs noted by palpation over tendons during active motion (flexion or extension) for 6 areas: hands, wrists, elbows, knees, ankles, and other areas. Joint tenderness index was determined as the sum of tenderness (rated 0–3) across 4 joints or joint areas (elbow, wrist, metacarpophalangeal, and knee) for both the left and right sides of the body (0–24). Joint swelling index was

calculated as the sum of swelling (rated 0–3) across the same 4 joints for both sides of the body (0–24). Joint contracture index represented a patient's loss of motion in wrist, elbow, and knee joints on both the right and left sides, ranging from 0 (no loss of motion) to 6 (loss of motion in all joint groups). Total tender points (0–18) was based on examination for 18 possible tender fibromyalgia points. In addition, patient self-reported symptoms were recorded (see Table 4). Patients were asked about presence/absence of a variety of symptoms in the month preceding the examination; medical terms were explained as necessary, or more patient-friendly terms were substituted (e.g., red spots for telangiectasia, lighter/darker skin for hypo/hyperpigmentation).

Patients also completed 3 questionnaires: HAQ-DI, HAQ-PVAS, and PAIS. The HAQ-DI[3] is a self-report measure that assesses patient function on a 0–3 scale. The HAQ-DI lists 20 activities across 8 categories and patients rate their difficulty in performing each activity on a 4-point scale (0 = without any difficulty to 3 = unable to do). The HAQ-DI is calculated by summing the highest score in each of the 8 categories and then dividing the sum by the number of categories answered (usually 8). The HAQ-DI is a valid measure of disability in patients with SSc[4-13]. For our study, internal consistency of the HAQ-DI, calculated as Cronbach's coefficient alpha, was 0.92, indicating excellent reliability. On the PVAS of the HAQ, patients rate their pain severity on a 15.0 cm VAS, with higher scores indicating more pain (possible range 0 = no pain to 3 = very severe pain). The HAQ-PVAS score has been validated for SSc[4,15].

The PAIS assesses psychological adjustment to disease[29,30]. Items on this 46-item self-report questionnaire are rated on a 4-point scale from 0 (not at all) to 3 (extremely), with higher scores indicating poorer adjustment. The PAIS yields 7 subscales: Health Care Orientation, Vocational Environment, Domestic Environment, Sexual Relationships, Extended Family Relationships, Social Environment, and Psychological Distress, as well as a Total score representing global adjustment. The reliability and validity of the PAIS have been established for SSc[15,31]. For our study, Cronbach's alpha for the PAIS Total score was 0.94, indicating excellent internal consistency. Cronbach's alphas for the 7 PAIS subscales were all acceptable: Health Care Orientation 0.69, Vocational Environment 0.85, Domestic Environment 0.82, Sexual Relationships 0.78, Extended Family Relationships 0.74, Social Environment 0.91, and Psychological Distress 0.87.

All analysis was conducted using SPSS 10.0 (SPSS, Chicago, IL, USA). Descriptive statistics are reported for sample demographics and all major study variables. Bivariate correlations (Pearson correlation coefficients if both variables were continuous, or point-biserial correlation coefficients if one variable was dichotomous) were calculated to examine simple relationships among variables. T-tests and one-way analyses of variance (ANOVA) were used to examine group differences on normally distributed interval data, and Mann-Whitney tests were used on categorical and non-normally distributed variables. Hierarchical multiple regression analysis was used to identify significant correlates of HAQ-DI, HAQ-PVAS, and PAIS, after controlling for skin score. Multiple regression analysis following procedures provided by Baron and Kenny[32] was used to test the 2 mediational models.

RESULTS

The final sample was composed of 114 patients with physician-confirmed diagnoses of SSc. All patients fulfilled American College of Rheumatology preliminary classification criteria for SSc[33]. Table 1 lists characteristics of the sample. Seventy-three (64%) patients had a diagnosis of dcSSc

Table 1. Demographic characteristics for the total sample (N = 114; 73 diffuse, 41 limited SSc).

Characteristic	Total	dcSSc	lcSSc
Mean age, yrs	49.50 (11.60)	49.22 (12.05)	50.01 (10.96)
Mean disease duration, yrs	4.30 (2.95)	4.31 (3.04)	4.27 (2.82)
	n (%)	n (%)	n (%)
Sex (%)			
Male	14 (12.3)	8 (11.0)	6 (14.6)
Female	100 (87.7)	65 (89.0)	35 (85.4)
Highest level of education completed (%)			
Some high school or below	11 (9.8)	9 (12.5)	2 (4.9)
High school graduate	23 (20.4)	17 (23.6)	6 (14.6)
College work/degree	63 (55.7)	40 (55.6)	23 (56.1)
Postgraduate work/degree	16 (14.2)	6 (8.4)	10 (24.4)
Ethnicity (%)			
Caucasian/European	81 (72.3)	52 (73.2)	29 (70.7)
African American	7 (6.3)	5 (7.0)	2 (4.9)
Latino/Hispanic American	11 (9.8)	7 (9.9)	4 (9.8)
Asian American/Pacific	5 (4.5)	4 (5.6)	1 (2.4)
Other	8 (7.1)	3 (4.2)	5 (12.2)
Yearly income (%)			
Under $10,000	8 (7.5)	5 (7.5)	3 (7.5)
$10,000 to $30,000	32 (29.9)	21 (31.3)	11 (27.5)
$30,000 to $50,000	29 (27.1)	19 (28.3)	10 (25.0)
Over $50,000	38 (35.5)	22 (32.8)	16 (40.0)
Marital status (%)			
Married/in committed relationship	81 (71.1)	53 (72.6)	28 (68.3)
Divorced/separated	20 (17.5)	11 (15.1)	9 (22.0)
Widow/widower	7 (6.1)	4 (5.5)	3 (7.3)
Never married	6 (5.3)	5 (6.8)	1 (2.4)

Means and SD are presented for age and disease duration.

(sclerodermatous skin induration distal as well as proximal to the elbows and knees, with or without facial involvement). The other 41 (36%) had a diagnosis of lcSSc (sclerodermatous skin induration distal, but not proximal, to the elbows and knees, with or without facial involvement). On average, patients had experienced their first non-Raynaud manifestation slightly more than 4 years earlier (mean 4.30, SD 2.95); there was no significant difference in disease duration between dcSSc and lcSSc patients (means 4.31 and 4.27 years, respectively). Comparisons between lcSSc and dcSSc patients showed no significant differences on demographic variables listed in Table 1, except that patients with lcSSc were more educated than those with dcSSc ($t(1,110) = 3.05$, $p < 0.005$).

Table 2 provides descriptive data from the patient self-report QOL measures. The HAQ-DI mean score (1.25) suggests somewhat greater disability than most previous SSc samples described in the literature[5,7,15,17], although similar to that described by Moser, *et al*[26]. The PVAS mean score (1.19) in the present sample, representing mild pain, is consistent with previous reports[15,17]. Total scores on the PAIS suggest psychosocial adjustment problems consistent with other patient populations (e.g., cancer patients[29,30]). Patients with dcSSc had significantly higher disability and pain scores than those with lcSSc; the groups did not differ on overall psychosocial adjustment (PAIS total score).

Table 3 shows the frequency of medical signs present on clinical examination as determined by the physicians. Means and standard deviations for MRSS and summary indices are presented, and significant differences between dcSSc and lcSSc patients are noted. Table 4 shows the frequencies of patient-reported medical symptoms, rated as present "within 1 month" of the examination date. Data for patients with dcSSc and lcSSc are presented, and differences indicated.

Bivariate correlations were used to examine relationships between physician-determined medical signs (listed in Table 3) and the 3 QOL outcomes (HAQ-DI, HAQ-PVAS, and PAIS). Skin score was significantly correlated with all 3 outcomes — with HAQ-DI ($r = 0.55$, $p < 0.001$), with HAQ-PVAS ($r = 0.47$, $p < 0.001$), and with psychosocial adjustment ($r = 0.30$, $p < 0.001$). In addition, for HAQ-DI, bivariate correlations showed that physician-assessed variables of joint tenderness ($r = 0.62$, $p < 0.001$), joint contracture ($r = 0.52$, $p < 0.001$), total tender points ($r = 0.29$, $p < 0.005$), tendon friction rubs ($r = 0.21$, $p < 0.05$), and muscle weakness ($r = 0.21$, $p < 0.01$) were all associated with significantly greater functional impairment. Joint swelling was the only physician-determined sign not significantly correlated with HAQ-DI ($p > 0.05$). For HAQ-PVAS, physician-assesssed joint tenderness ($r = 0.46$, $p < 0.001$), total tender points ($r = 0.36$, $p < 0.001$), and joint contractures ($r = 0.27$, $p < 0.005$) were significantly associated with more pain. Higher (worse) PAIS scores were significantly related to physician-assessed variables of joint tenderness ($r = 0.30$, $p < 0.001$), joint contractures ($r = 0.20$, $p < 0.05$), and higher total tender points ($r = 0.19$, $p < 0.05$).

Table 2. Means and standard deviations for HAQ-DI, HAQ-PVAS, and PAIS scores.

Measure	Total, mean	Total, SD	dcSSc, mean	dcSSc, SD	lcSSc, mean	lcSSc, SD
HAQ Disability Index (HAQ-DI)	1.25	0.77	1.43	0.79	0.92	0.60[a]
HAQ Pain Score (HAQ-PVAS)	1.19	0.83	1.37	0.86	0.87	0.67[b]
PAIS raw scores						
Total	45.40	21.41	48.00	20.03	40.67	23.24
Health care orientation	7.41	3.62	7.46	3.52	7.31	3.84
Vocational environment	6.83	4.54	7.73	4.30	5.18	4.56[c]
Domestic environment	7.88	4.66	8.03	4.27	7.62	5.33
Sexual relationships	6.57	3.89	7.07	3.63	5.67	4.24
Extended family relationships	2.42	2.72	2.55	2.53	2.18	3.06
Social environment	6.62	5.00	7.31	5.21	5.36	4.39[d]
Psychological distress	7.67	4.42	7.85	4.51	7.36	4.29
PAIS T-scores						
Total	51.87	11.13	53.46	10.61	48.97	11.60
Health care orientation	47.55	9.91	47.72	9.57	47.23	10.61
Vocational environment	53.24	10.94	55.35	9.90	49.38	11.80
Domestic environment	50.36	11.27	51.39	10.48	48.49	12.52
Sexual relationships	54.80	8.05	55.77	7.42	53.03	8.93
Extended family relationships	50.35	9.36	51.34	8.85	48.54	10.09
Social environment	50.85	11.17	52.34	11.46	48.15	10.22
Psychological distress	51.62	8.79	51.90	9.01	51.10	8.79

[a] Significant difference, dcSSc versus lcSSc subgroups: $t(1, 112) = -3.61$, $p < 0.001$. [b] Significant difference, dcSSc versus lcSSc subgroups: $t(1, 100) = -3.47$, $p < 0.001$. [c] Significant difference, dcSSc versus lcSSc subgroups: $F(1, 108) = 8.50$, $p < 0.005$. [d] Significant difference, dcSSc versus lcSSc subgroups: $F(1, 108) = 3.93$, $p < 0.05$.

Table 3. Physician-determined medical signs present on physical examination, including summary indices. Percentage of sample is followed by number of subjects (n). Means are followed by standard deviations (SD).

	Total	dcSSc	lcSSc
Finger/hand edema	42.5 (48)	38.9 (28)	48.8 (20)
Pitting scars of digits	5.3 (6)	2.7 (2)	9.8 (4)
Digital tip ulcers	14.0 (16)	15.1 (11)	12.2 (5)
Ulcers in other locations	25.4 (29)	34.2 (25)	9.8 (4)[a]
Tendon friction rubs (any)	15.2 (17)	19.2 (13)	10.0 (4)
Pulmonary	2.6 (3)	1.4 (1)	4.9 (2)
Cardiac	1.8 (2)	1.4 (1)	2.4 (1)
Summary indices, mean (SD)			
Modified Rodnan Skin Score (0–51)	16.52 (10.05)	21.16 (8.95)	8.24 (5.62)[b]
Proximal muscle weakness (0–4)	0.62 (0.83)	0.65 (0.82)	0.56 (0.85)
Tendon friction rubs (0–6)	0.25 (0.72)	0.32 (0.84)	0.13 (0.40)
Joint tenderness index (0–24)	4.25 (5.49)	5.75 (6.24)	1.70 (2.27)[c]
Joint swelling index (0–24)	1.03 (2.12)	1.12 (2.48)	0.88 (1.31)
Joint contracture index (0–6)	1.26 (1.49)	1.61 (1.59)	0.64 (1.04)[d]
Total tender points (0–18)	7.14 (5.20)	8.03 (5.50)	5.50 (4.18)[e]

[a] Significant difference, dcSSc versus lcSSc subgroups: $t(1, 110.49) = -3.35$, $p < 0.001$. [b] Significant difference, dcSSc versus lcSSc subgroups: $t(1, 110.53) = -9.45$, $p < 0.0001$. [c] Significant difference, dcSSc versus lcSSc subgroups: $t(1, 92.46) = -4.84$, $p < 0.001$. [d] Significant difference, dcSSc versus lcSSc subgroups: $t(1, 104) = -3.81$, $p < 0.001$. [e] Significant difference, dcSSc versus lcSSc subgroups: $t(1, 94.41) = -2.68$, $p < 0.01$.

Relationships of patient-reported medical symptoms to the 3 QOL outcomes are shown in Table 4. For each symptom, we divided patients into groups based on whether they endorsed the symptom as present or absent during the past month, and used one-way ANOVA to see if these groups differed on QOL outcomes. Significant ANOVA ($p < 0.05$) are indicated in the far right column; in all cases, the presence of the symptom was associated with worse QOL.

Hierarchical multiple regression analysis was used to identify significant correlates of HAQ-DI, HAQ-PVAS, and PAIS, after controlling for skin score. For each equation, MRSS was entered in the first step as an overall index of disease severity. In the second step, signs and symptoms were entered that were significant correlates in bivariate analysis. Results are shown in Table 5. After controlling for skin score, physician-assessed joint tenderness and total tender points, and patient-reported joint pain on motion, joint contracture, dependent edema, extremity cutaneous ulcers other than on the fingers, and dyspnea were significant correlates of HAQ-DI. After controlling for skin score, significant correlates of HAQ-PVAS were patient-reported dependent edema and joint tenderness. After controlling for skin score, patient-reported postprandial bloating, joint pain on motion, and dependent edema were significant correlates of PAIS.

Finally, multiple regression analysis was used to test 2 models: (1) HAQ-DI and -PVAS mediate the relationship between disease severity (skin score) and PAIS; and (2) HAQ-PVAS and PAIS mediate the relationship between disease severity (skin score) and HAQ-DI. According to guidelines provided by Baron and Kenny[32], 3 conditions must be met for a given variable to be said to function as a mediator: (1) the predictor variable (MRSS) must be related to the outcome variable (PAIS); (2) the predictor variable (MRSS) must be related to the potential mediator; and (3) the mediator must be related to the outcome variable after controlling for the predictor variable (MRSS). The test of mediation is whether the significant effect of the predictor on outcome becomes nonsignificant once the mediator is controlled. Results of regression analysis showed that these conditions were met for the first model, but not the second. For the first model (Figure 1), simple regression analyses of conditions 1 and 2 showed that MRSS was a significant predictor of the outcome variable PAIS ($F(1, 108) = 10.26$, $p < 0.005$), and also a significant predictor of both potential mediators, HAQ-DI ($F(1, 108) = 45.41$, $p < 0.001$) and -PVAS ($F(1, 108) = 27.03$, $p < 0.001$). Then, 2 separate regression analyses were used to test the presence of mediation (condition 3). The first regression analysis showed that the relationship between MRSS and PAIS was mediated by HAQ-DI ($F(2, 107) = 37.99$, $p < 0.001$), in that the relationship between MRSS and PAIS became nonsignificant after HAQ-DI was accounted for. The second regression analysis showed similar findings: the relationship between MRSS and PAIS was mediated by HAQ-PVAS ($F(2, 107) = 30.82$, $p < 0.001$), in that the relationship between MRSS and PAIS became nonsignificant after HAQ-PVAS was accounted for. For the second model, condition 3 was not met; the relationship between MRSS and HAQ-DI did not become nonsignificant after accounting for either HAQ-PVAS or PAIS.

DISCUSSION

This study identified physician-determined and patient-reported medical correlates of 3 SSc-related QOL outcomes: disability, pain, and psychosocial adjustment. As expected, over-

Table 4. Presence of patient-reported symptoms within 1 month of physical examination, and relationship to HAQ-DI, HAQ-PVAS, and PAIS scores. In all cases where symptoms are related to outcomes, the presence of symptoms is associated with poorer outcomes.

	Total % (N)	dcSSc % (N)	lcSSc % (N)	Outcome Significantly Related to Symptom Presence/Absence ($p < 0.05$)
Raynaud's	78.1 (89)	79.5 (58)	75.6 (31)	
Hand edema	51.8 (59)	52.1 (38)	51.2 (21)	DI, PVAS
Hyperpigmentation	61.4 (70)	67.1 (49)	51.2 (21)	DI, PVAS
Hypopigmentation	51.8 (59)	53.4 (39)	48.8 (20)	DI
Digital ulcers	32.5 (37)	32.9 (24)	31.7 (13)	DI, PAIS
Other extremity ulcers	10.5 (12)	12.3 (9)	7.3 (3)	DI, PAIS
Calcinosis	13.2 (15)	12.3 (9)	14.6 (6)	DI
Telangiectasias	60.5 (69)	60.3 (44)	61.0 (25)	
Morning stiffness[a]	58.8 (67)	67.1 (49)	43.9 (18)	DI, PVAS
Joint pain on motion	61.4 (70)	63.0 (46)	58.5 (24)	DI, PVAS, PAIS
Joint tenderness	60.5 (69)	64.4 (47)	53.7 (22)	DI, PVAS, PAIS
Joint contracture[b]	50.9 (58)	60.3 (44)	34.1 (14)	DI, PVAS, PAIS
Muscle pain	49.1 (56)	53.4 (39)	41.5 (17)	DI, PVAS, PAIS
Muscle weakness[c]	50.0 (57)	58.9 (43)	34.1 (14)	DI, PVAS, PAIS
Dyspnea	36.0 (41)	35.6 (26)	36.6 (15)	DI, PAIS
Orthopnea	9.6 (11)	12.3 (9)	4.9 (2)	PAIS
Pleuritic pain	8.8 (10)	9.6 (7)	7.3 (3)	
Palpitations	28.1 (32)	32.9 (24)	19.5 (8)	DI, PVAS, PAIS
Dependent edema	27.2 (31)	32.9 (24)	17.1 (7)	DI, PVAS, PAIS
Dysphagia	44.7 (51)	42.5 (31)	48.8 (20)	PAIS
Pyrosis	59.6 (68)	60.3 (44)	58.5 (24)	PAIS
Postprandial bloating	36.0 (41)	37.0 (27)	34.1 (14)	PAIS
Abdominal pain	23.7 (27)	23.3 (17)	24.4 (10)	
Diarrhea	33.3 (38)	30.1 (22)	39.0 (16)	
Constipation	33.3 (38)	32.9 (24)	34.1 (14)	
Dry eyes	34.2 (39)	37.0 (27)	29.3 (12)	DI, PVAS, PAIS
Dry mouth	43.0 (49)	45.2 (33)	39.0 (16)	DI
Impotence (male only)	3.5 (4)	2.7 (2)	4.9 (2)	

[a] Significant difference, dcSSc versus lcSSc subgroups: $t(1, 73.31) = -2.24$, $p < 0.05$. [b] Significant difference, dcSSc versus lcSSc subgroups: $t(1, 110) = -2.71$, $p < 0.01$. [c] Significant difference, dcSSc versus lcSSc subgroups: $t(1, 111) = -2.47$, $p < 0.05$. DI: HAQ Disability Index; PVAS: HAQ pain visual analog scale; PAIS: Psychosocial Adjustment to Illness Scale total score.

all disease severity, operationalized as physician-determined skin score, was a strong significant correlate of both disability and pain. This finding is consistent with previous studies that have consistently shown a positive relationship between skin changes and disease-associated disability and pain.

After accounting for skin score, other significant correlates of disability (but not pain) were physician-assessed joint tenderness and number of tender points, patient self-reported joint pain on motion, limitation of joint motion, extremity ulcers other than those on the fingers, and dyspnea. Patient-reported joint tenderness was a significant correlate of pain only. This pattern of results is consistent with previous findings that joint pain and tenderness, whether determined through physician examination or reported by patients, are associated with functional disability and pain. For example, changes in swollen joint counts over 2 years in a prospective study of patients enrolled in the D-penicillamine trial were among the strongest predictors of changes in HAQ-DI scores over the same time period[7]. Interestingly, patient report of the specific symptom of dependent edema ("Do your lower legs swell at night?") was a significant correlate of both disability and pain (and of psychosocial adjustment, see below); indeed, it was the strongest correlate of SSc-related pain after accounting for skin score. Although the lower leg swelling is likely the effect of sensitization resulting from skin thickening, the presence of lower leg swelling accounts for significant variance, especially in patient-reported pain, after skin thickening has already been accounted for. Dependent edema may represent a symptom that is particularly challenging and painful for patients or that correlates with other signs and symptoms that are particularly distressing. Specific attention from physicians could prove beneficial not only to reducing edema or lower leg swelling but also to alleviating disability and pain.

The significant but small relationship between skin score and psychosocial adjustment is also consistent with existing research literature. Studies of psychosocial aspects of disease have consistently found that disease severity, although signif-

Table 5. Hierarchical regression analysis predicting disability, pain, and adjustment.

Variables in Equation	Beta[1]	Change in R square[2]	Significance
Correlates of disability, total R square = 0.62, F (8, 85) = 19.90, p < 0.0001			
MRSS[a]	0.55	0.29	p < 0.0001
Joint tenderness index[a]	0.47	0.18	p < 0.0001
Joint pain on motion[b]	0.24	0.04	p < 0.01
Joint contracture[b]	0.20	0.03	p < 0.05
Dependent edema[b]	0.17	0.02	p < 0.05
Extremity ulcers other than on fingers[b]	0.17	0.02	p < 0.05
Dyspnea[b]	0.16	0.02	p < 0.05
Total tender points[a]	–0.17	0.02	p < 0.05
Correlates of pain, total R square = 0.41, F (3, 91) = 22.64, p < 0.0001			
MRSS[a]	0.45	0.20	p < 0.0001
Dependent edema[b]	0.39	0.13	p < 0.0001
Joint tenderness[b]	0.30	0.06	p < 0.001
Correlates of psychosocial adjustment, total R square = 0.42, F (4, 93) = 18.19, p < 0.0001			
MRSS[a]	0.30	0.08	p < 0.01
Postprandial bloating[b]	0.45	0.20	p < 0.0001
Joint pain on motion[b]	0.34	0.11	p < 0.0001
Dependent edema[b]	0.20	0.03	p < 0.05

[1] Beta on entry; [2] variance accounted for when predictor enters equation. [a] Clinical features detected in physician examination; [b] patient self-reported symptom.

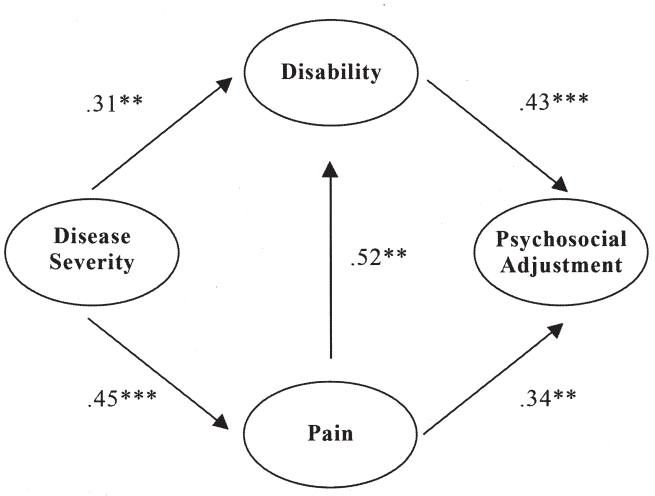

Figure 1. Mediational model of the relationship between disease severity and psychological adjustment to illness, with disability and pain mediating the relationship. Path coefficients based on standardized betas are shown. **p < 0.0005; ***p < 0.0001.

icantly associated with adjustment problems, is not a strong correlate. It is interesting that several patient-reported symptoms emerged as significant correlates of maladjustment. Patients who reported postprandial bloating, joint pain on motion, or dependent edema were more likely to be experiencing difficulty adjusting to their disease. Postprandial bloating was the strongest correlate of adjustment problems, explaining 20% of the variance, compared to the 8% explained by skin score. This suggests that bloating after eating may be particularly distressing to patients in terms of its impact on QOL or that this symptom may be a surrogate for more general GI involvement, since there were few other GI-specific questions. The reasons for this were not explored in this study, but merit further investigation. Medical and/or behavioral interventions that could reduce post-meal bloating may prove helpful in improving QOL for patients with SSc.

Regression analysis supported a mediational model in which disease severity directly influences disease-related disability and pain, which in turn affect psychosocial adjustment. An alternative model, in which disease-related pain and psychosocial adjustment were considered as mediators of the relationship between disease severity and disability, was not supported. Although the cross-sectional data presented here preclude definitive causal interpretations, the findings raise the possibility that disability and pain may be the more important points for direct intervention, and that intervening in these areas may be particularly effective in reducing difficulties in psychosocial QOL. Although rheumatologists may be frustrated in their efforts to stop or reduce SSc skin changes, interventions to reduce functional disability and pain experiences may improve patient QOL in the absence of actual changes in disease pathology. For example, patient self-management programs for rheumatoid arthritis have shown promise in decreasing pain, disability, fatigue, and physician visits[34-36]. These programs are just beginning to be used in SSc[1,2,37]. Other psychosocial interventions such as cognitive-behavioral interventions have also shown effectiveness in pain management for chronic illness, and are being tested for SSc[1,2].

Our results underscore the importance of a skin score examination to determine MRSS, and suggest that having patients complete a brief self-report questionnaire asking them to identify which specific common symptoms of SSc

they have recently experienced would be a simple and time-efficient way of identifying patients who have difficulties with functioning and/or adjustment problems. Pincus and colleagues have demonstrated the efficacy and efficiency of this approach in rheumatoid arthritis, showing that brief patient self-report questionnaires are as sensitive to treatment effects as more traditional (and expensive) physical and laboratory assessments[38]. They introduced the Multidimensional HAQ (MDHAQ), which includes the modified HAQ along with psychological items, VAS for pain and fatigue, and the Rheumatology Attitudes Index[39]. The MDHAQ has not been specifically validated for SSc, but the instrument performed well in a large sample of consecutive rheumatology patients that included 16 patients with SSc. Although screening with self-report questionnaires may seem cumbersome to already overtaxed rheumatology practices, a recent study found that self-report questionnaires were viewed as beneficial and easy to use by rheumatologists who introduced them in their practices after undergoing a training course in their use[40]. There have been numerous calls for regular use in clinical practice of the easily-completed HAQ; a brief checklist of common SSc symptoms for patients to endorse could supplement this approach.

Our study had several limitations. The sample was voluntary, recruited through patient registries, and did not consist of consecutive patients or admissions. The 3 participating medical centers are all located in urban settings on the West Coast of the United States. Measurement of medical variables was limited to those typically assessed during a routine SSc clinical examination and more sophisticated technology was not employed (e.g., routine echocardiograms on all patients at the time of the examination for this study). The major outcome variables were all assessed via patient self-report, and although this is not atypical, it would be useful to have corroborating reports from other observers. Multiple comparisons and statistical tests inflated Type 1 error rate. Finally, the data presented here are cross-sectional. Future research should examine patient outcomes at multiple timepoints, to determine what baseline variables might predict future outcomes and to clarify causal relationships. It would be especially important to follow patients from time of diagnosis, utilizing a comprehensive clinical and QOL assessment covering multiple domains. It is possible that overall disease severity, as represented by MRSS, may be less central than currently perceived, especially in terms of predicting psychosocial outcomes. Closer examination of the relationship of specific disease-related signs and symptoms to functional and psychosocial outcomes over time could help rheumatologists identify important targets of intervention for improving patient quality of life.

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